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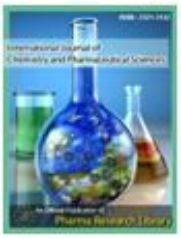

Review Article Open Access

Synthesis of Thiazole Derivatives-A Review

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A B S T R A C T

A number of heterocyclic derivatives containing nitrogen have been used as versatile scaffolds in drug development. Thiazole is one of the heterocyclic compounds with remarkable pharmacological activities. Thiazole derivatives were found to possess the biological activities like anti-convulsant, anti-microbial, anti-inflammatory, anti-cancer, anti-HIV, anti-diabetic, anti-alzheimer, anti-hypertensive, anthelmintic and anti-oxidant activities. Due to its biological activities it has great pharmaceutical importance; hence, synthesis of this compound is of considerable interest. This review mainly focuses on the research work reported in the scientific literature on different synthetic procedures of Thiazole compounds.

Keywords: Synthesis, substituted thiazole, Thiazole derivatives.

A R T I C L E I N F O

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1. Introduction

Natural products play an important role in the development of new drugs[1] and provide the inspiration to develop new strategies toward the diversity-oriented synthesis of novel smallmolecule libraries. An extraordinary group of biologically active natural products, often from a marine environment,[2] contains bis-thiazoles, bis-oxazoles and bis-

oxazol-thiazole systems, which are derived from biosynthetic cyclizations of precursor amino acids Cys, Ser and Thr.[3] Thiazoles are of eminent importance because of their potential as bioactive compounds[4] and versatile building blocks for natural products and pharmaceuticals. Thiazole heterocycles are important subunits in many complex natural compounds and drugs, *e.g.* Vitamine B1, Epothilones, Thiostrepton, Niza-tidine (ulcer therapeutic), Ritonavir (a potent inhibitor of HIV protease) (Fig. 1) and thiamine pyrophosphate (TPP, a coen-zyme that is part of the Krebs cycle in the process of cellular respiration).[5] Further, there are many other applications of thiazole derivatives, for example in liquid crystals or cosmetics (sunscreens).[6]

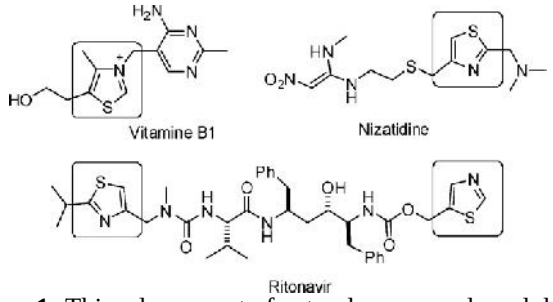
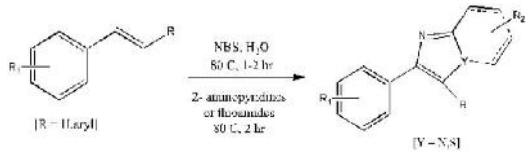


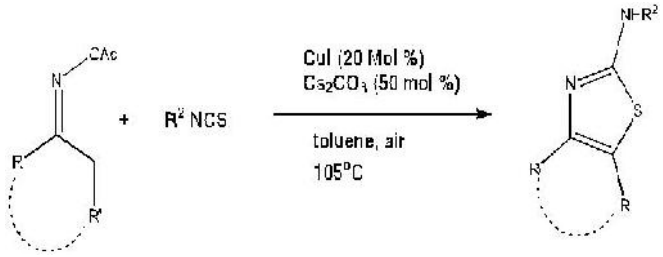
Figure 1: Thiazoles as part of natural compounds and drugs

2. Synthesis of Thiazole Derivatives

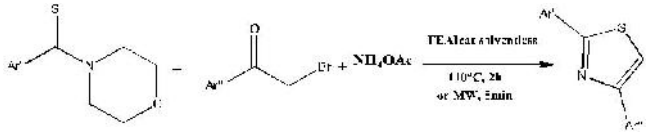
Shinde M et al. [7] reported a one pot synthesis of substituted imidazo-pyridines and thiazoles from styrenes in water assisted by NBS. Heating of commercially available styrenes with NBS in water followed by reaction with 2-aminopyridines or thioamides afforded important heterocyclic scaffolds in a one pot procedure. The reaction proceeds via co-oxidant free, in situ formation of α-bromoketone using NBS as a bromine source as well as an oxidant followed by trapping with suitable nucleophiles to provide imidazopyridines and thiazoles.



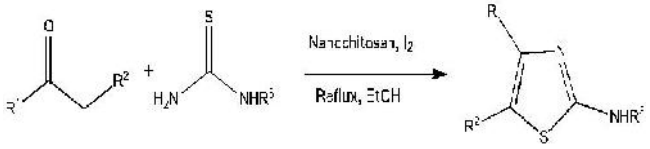
Tang X et al. [8] synthesized 4-substituted and 4, 5-disubstituted 2-aminothiazoles via the copper-catalyzed coupling of oxime acetates with isothiocyanates. This process involved copper-catalyzed N–O bond cleavage, activation of vinyl sp2 C–H bonds, and C–S/C–N bond formations.



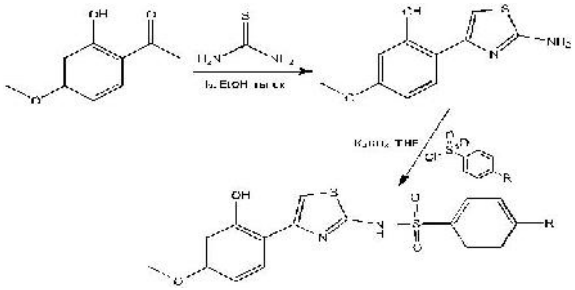
Zali-boeini H et al.[9] developed a novel one-pot three-component reaction for the synthesis of thiazole derivatives from thioamides, α-haloketones and ammonium acetate at 110 °C and/or under microwave irradiation under solvent-free conditions**.**



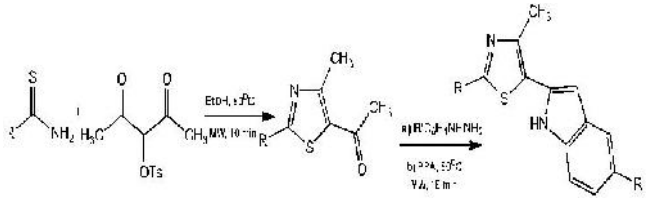
Safari J et al.[10] reported an efficient method for the synthesis of 2-aminothiazoles by one-pot reaction of ketone and thiourea using biodegradable, green catalyst nanochitosan under mild condition.



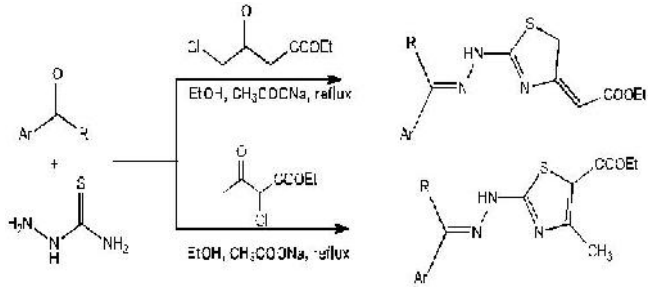
Tsai CY et al.[11] reported the synthesis of paeonol-2-aminothiazole from paeonol, thiourea and iodine by condensation-cyclization of thiourea initiated by iodine and extended the synthetic work for paeonol-2-aminothiazole-phenylsulfonyl derivatives by treating 2-aminothiazole-paeonol with substituted phenylsulfonyl chloride.



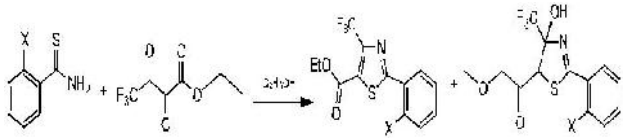
Vaddula BR et al.[12] reported synthesis of a series of 5-(2′-indolyl)-thiazoles from the reaction of thioamides with 3-tosyloxypentane-2,4-dione led to in situ formation of 5-acetylthiazole which upon treatment with arylhydrazines in polyphosphoric acid.



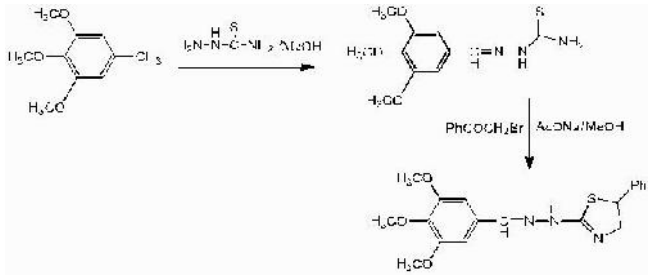
Xiabing M et al. [13] developed an efficient and environmentally benign reaction process for the synthesis of a series of hydrazinyl-4-methylthiazole compounds via one-pot three-component reaction of aldehyde/ketone, thiosemicarbazide and chlorinated β-keto ester catalyzed by anhydrous sodium acetate in ethanol solvent.



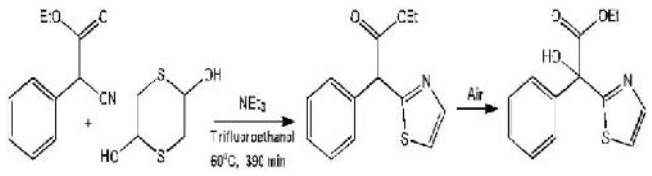
Xicai W et al.[14] reported the synthesis of series of novel 2-phenyl-4-trifluoromethyl thiazole-5-carboxamide derivatives from 2-halobenzothioamide and ethyl 2-chloro-4,4,4-trifluoro-3-oxobutanoate then evaluated for their anticancer activity.



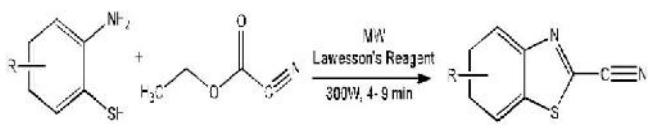
A.I El Shenavy et al.[**15]** reported the synthesis of 5-Phenyl-2-[(3, 4, 5-trimethoxybenzylidene)-hydrazino]-thiazole by cyclization of 1-[(3,4,5-trimethoxy benzyliden) amino]-thiourea with phenacyl bromide in the presence of fused sodium acetate.



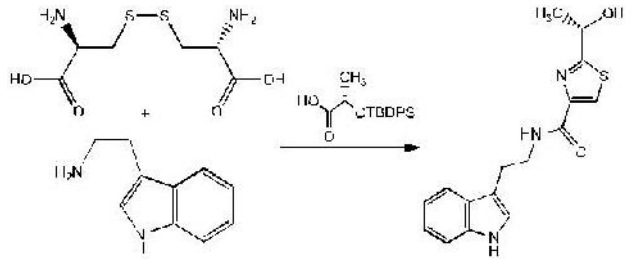
CJ et al.[16] reported synthesis of the thiazole derivatives by spontaneous aerobic oxidation of ethyl 2-phenyl-2-(thiazol-2-yl)-acetate.



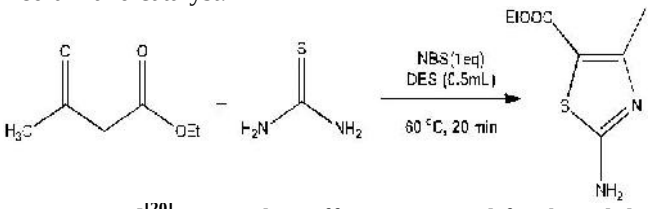
Prajapati N et al.[17] described a one-step synthesis of various substituted 2-cyanobenzothiazole by condensation of corresponding substituted ortho-aminothiophenol with ethyl cyanoformate, employing an effective amount of Lawesson's Reagent, under microwave irradiation (MWI) and solvent free conditions within short period of time (4-9 min.).



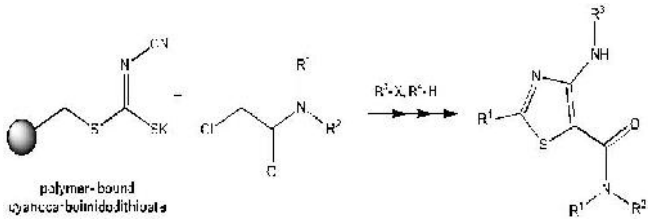
Sun X et al.[18] reported the synthesis of the natural product bacillamide B, starting from L-cystine by one-pot four-step process of thiazoline formation via a cascade disulfide cleavage/ thiocarbonylation/Staudinger reduction / aza-Wittig reaction using β-azido disulfide and carboxylic acid as substrates.



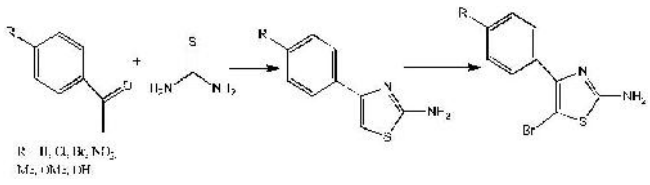
Azizi N et al.[19] reported a deep eutectic solvent assisted one pot synthesis of 2-amino-thiazole from the three-component reactions of active methylene compounds, urea or thiourea and N-bromosuccinimide (NBS) in the choline chloride–urea-based deep eutectic solvent (DES) reaction medium and catalyst.



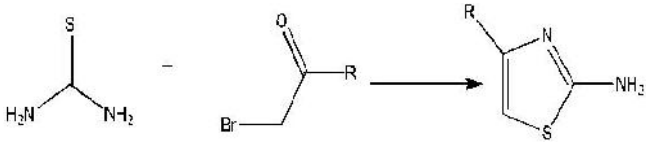
Dong D et al[20] reported an efficient protocol for the solid-phase synthesis of 2,4-disubstituted 5-carbamoyl-thiazole derivatives by the. Thorpe-Ziegler type cyclization of 2-chloroacetamide,polymer bound cyanocarboimidodithioate, which is derived from Merrifield resin.



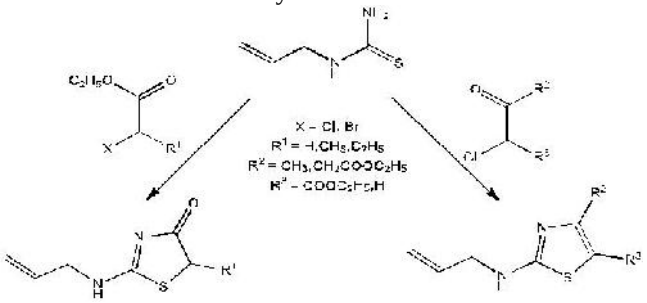
Castell R.M. et al.[21] reported synthesis of a 2-amino-4-arylthiazoles from acetophenone and thiourea under microwave irradiation.



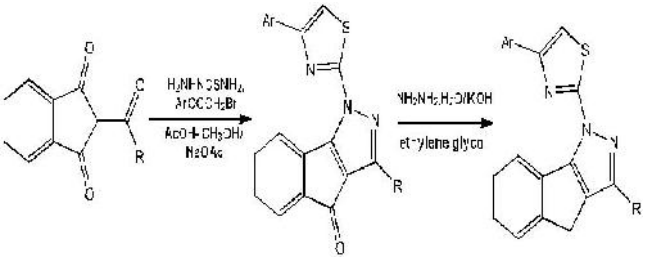
Valiveti A.K. et al [22] reported synthesis of 4-substituted-2- amino thiazoles from thiourea and bromo-acetaldehyde derivative.



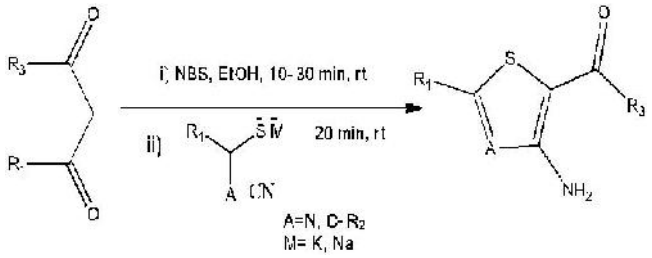
Studzinska R et al [23] reported the synthesis of thiazole and 4, 5-dihydrothiazole derivatives from chlorooxoesters and haloesters with a 1-allylthiourea in methanol.



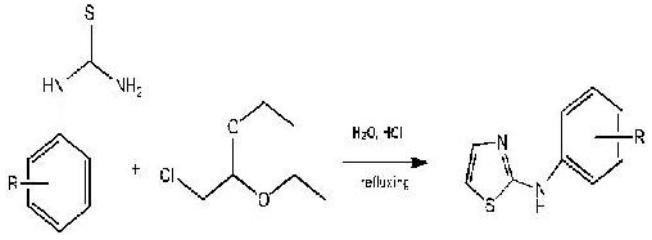
Mor S et al[24] reported a convenient one-pot synthesis of new thiazole tethered indeno-[1,2-c]-pyrazol-4-ones by three-component reaction between 1,3-diketones, thiosemicarbazide and α-bromoketones. Wolff-Kishner reduction of indeno-[1,2-c]pyrazol-4-ones led to the formation of corresponding indeno-[1,2-c]-pyrazoles.



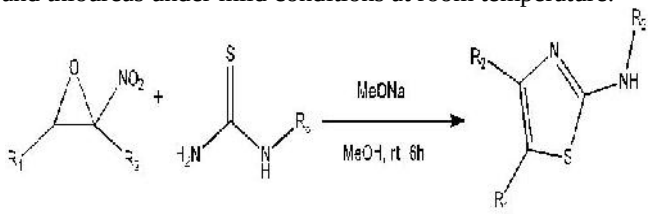
Luo L et al[25] described NBS-mediated sequential one-pot synthesis of multi- functionalized thiazoles and thiophenes from 1,3-dicarbonyl compounds and mercaptonitrile salts. This transformation involves sequential bromination /SN2 alkylation/Thorpe–Ziegler cyclization/regio-selective elimination of a –COR group, affording the desired products in moderate to good yields. The sequence of the leaving reactivity of –COR groups was determined and a possible mechanism was proposed.



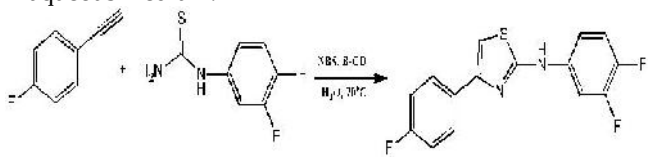
Babar A et al [26] synthesized anilinothiazoles by acid catalyzed condensation of N-phenylthioureas and 2-chloro-1,1-dimethoxyethane. Substituted anilines were employed to introduce substitution in 2-anilinothiazoles.



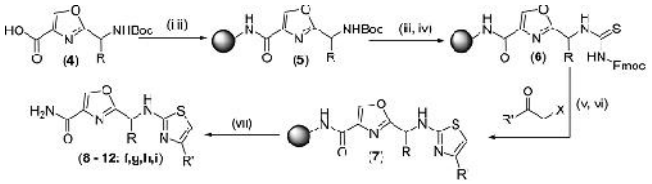
Zhao D et al [27] developed an efficient synthesis of 2,4,5 - trisubstituted thiazoles via the reaction of α-nitroepoxides and thioureas under mild conditions at room temperature.



Madhav B et al[28] developed a one-pot synthetic procedure for the synthesis of thiazoles from alkynes and 1-(3,4-difluorophenyl)-thiourea catalyzed by β-cyclodextrin in aqueous medium.

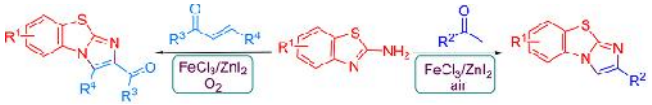


Adel Nefzi et al[29] developed combinatorial library of novel oxazol-thiazole bis-heterocycles in excellent yields with high purity using a solution and solid-phase parallel synthesis approach. Oxazole amino acids, prepared from serine methyl ester and amino acids via coupling and cyclodehydration, were treated with Fmoc-NCS and α-haloketones for the parallel synthesis of diverse bis-heterocycles. Fmoc- isothiocyanate is used as a traceless reagent for thiazole formation.

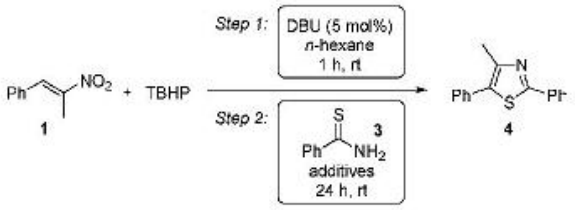


Reaction conditions: (i) MBHA resin, DIEA, DCM, 5 min; (ii) HOBt, DIC, DMF, overnight; (iii) 55% TFA in DCM, 30 min; (iv) Fmoc-NCS (3equiv), 10 h; (v) Piperidine/DMF (20%), 10 min; (vi) Halo ketone, DMF, 80 °C; (vii) HF-cleavage.

Alakananda Hajra et al [30] developed FeCl3/ZnI2-catalyzed aerobic oxidative cyclization between 2-aminobenzothiazole and ketone/chalcone for the synthesis of benzo[d]imidazo[2,1-b]thiazole. A variety of fused benzoimidazothiazole derivatives are obtained by this protocol.



Svetlana B. Tsogoeva et al [31] developed a novel one-pot process providing a practical route for the formation of 1,3-thiazoles from nitro-olefins. The use of commercially available DBU as an organocatalyst for the epoxidation of nitro-olefins with TBHP, followed by the reaction with thiobenzamides, and the very mild conditions used for both transformations, make this process a simple and convenient approach to obtain thiazole heterocycles



4. Conclusions

Review of synthetic schemes which have been developed in about 20 years of research by the use of thiazole-based methodology may serve to illustrate the potential of this approach in synthetic programs toward the construction of complex systems or special molecular fragments. The type and variety of the classes of compounds which were accessible by this methodology demonstrate its wide scope and utility. This was primarily due to a small arsenal of readily accessible thiazole-armed reagents and their effective carbon-carbon bond-forming reactions. The synthetic utility of the thiazole-based methodology has been sufficiently established through the examples reported in this review and its scope should be expanded in the future. From the same examples it is apparent that the use of the thiazole ring as synthetic auxiliary allows a great deal of potential chemistry compatibility problems to be avoided, which may be a great obstacle to the execution of synthetic programs directed toward the preparation of densely functionalized chiral systems. In fact, the thiazole ring appears to be endowed with some properties which make it a very convenient tool in synthetic methodology. Specifically, it withstands a great deal of chemistry throughout the elaboration of the substrate in which it has been introduced, but it can be rapidly and efficiently immolated to give the formyl group by a procedure which is well tolerated by a wide variety of functional groups and does not affect existing stereocenters.

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